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Assessment of left ventricle diastolic function in myocardial infarction patients treated with primary angioplasty

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Abstract

Background: *More than 5% of patients over the age of 65 have been found to develop heart failure, and over half of them preserve normal left ventricular systolic function. In the last few years, diastolic heart failure has become a serious clinical and epidemiological problem.*

Methods: *This prospective study was carried out on 99 patients. Patients were evaluated up to three months after primary percutaneous coronary intervention (PCI). Evaluation was performed three times: within the first 24 hours after primary PCI, on day seven after PCI and at three months after PCI. We analyzed the relationship between the severity of left ventricle diastolic dysfunction and atherosclerosis risk factors, infarction site, maximum levels of cardiac biomarkers such as troponin I, CPK and CK-MB, CRP protein levels, angioplasty effectiveness, reperfusion time, TIMI and TMPG grade.*

Results: *Most patients with ST elevation myocardial infarction (STEMI) treated with primary PCI demonstrated left ventricle diastolic dysfunction on the first day of myocardial infarction. Levels of cardiac biomarkers were significantly higher in patients with restrictive filling pattern. The inflammatory response (CRP levels) was found to have an important role in the development of diastolic abnormalities. There was a close relationship between diastolic and systolic function. Average values of left ventricular ejection fraction in patients with restrictive filling pattern were significantly lower than in those with impaired relaxation (44.7* vs. *52.7%; $p < 0.001$) and normal filling (54.2%; $p = 0.002$).*

Conclusions: *More than half of patients with a first STEMI have left ventricle diastolic dysfunction within the first day after PCI, and these abnormalities are still present three months after PCI. Time and effectiveness of reperfusion, CRP level, troponin I, max, CPK max and CK-MB max levels as well as left ventricular ejection fraction have an important influence on the development of diastolic dysfunction. Infarct extension contributes significantly to the process.* (Cardiol J 2009; 16, 5: 440–446)

Key words: heart failure, diastolic function, ST elevation myocardial infarction, primary angioplasty

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Introduction

Heart failure (HF) continues to be one of the leading causes of hospitalization in cardiology wards worldwide. Typically, it is associated with impaired systolic function of the left ventricle (LV). Epidemiological evidence suggests that 40–50% of patients with HF symptoms have preserved systolic function [1–3]. Thus, in recent years, diastolic HF has become an important clinical problem. Isolated diastolic HF is defined as a condition in which elevated filling pressures of the left ventricle cause abnormal elevation of end-diastolic pressures followed by typical clinical HF manifestations with preserved systolic function of LV [4, 5].

Measurement of left ventricle diastolic function in hypertensive or acute coronary syndrome patients is a useful tool for prediction of mortality and the development of heart failure. There is evidence showing the role of a restrictive LV filling pattern as a negative prognostic factor. Its impact has been confirmed in the acute phase of myocardial infarction (MI), amyloidosis, dilated cardiomyopathy, and also in patients selected for heart transplantation [6–8]. Acute ischemia and necrosis during MI and duration of reperfusion time have a serious influence on LV filling parameters after the infarction [8–10]. There is no clear data describing changes of left ventricular filling parameters in patients after myocardial infarction treated with primary percutaneous coronary intervention (pPCI).

The aim of this study is to evaluate left ventricular diastolic function in patients treated with pPCI for a first MI and its correlation with comorbidities, infarction site, reperfusion time, PCI effectiveness rate, necrosis area, development of the collaterals and selected echocardiographic parameters.

Methods

Inclusion criteria were as follows: diagnosis of a first myocardial infarction with ST-elevation (ESC guidelines), sinus rhythm in echocardiography (ECG), age between 30 and 70 years, good 'acoustic window' and a patient's informed consent. Patients with diabetes, primary cardiomyopathy, suspicion of amyloidosis and patients with mitral regurgitation of grade 2 or higher were excluded.

This prospective study was carried out on 104 patients ranging in age from 33 and 70 with ST elevation myocardial infarction (STEMI) treated with primary angioplasty during the period 2004––2006. Patients were evaluated up to three months after primary PCI. The study was completed by 99 patients: 79 men (79.8%) and 20 women (20.2%) aged between 33 and 70 (mean 54.7 ± 7.85 years). Clinical and echocardiographic evaluation was performed three times: within the first 24 hours after primary PCI (E_1), on the seventh day after PCI (E_7) and finally three months after the procedure (E_{90}). LV filling pattern was assessed according to the Canadian Cardiology Society criteria. Normal pattern (profile A), impaired relaxation (profile B) and pseudonormal or restrictive pattern (profile C) were allocated [11]. Analysis of the pulmonary venous flow velocity was performed in order to differentiate normal filling from pseudonormal pattern.

Patients were divided into two groups: those with anterior wall MI and inferior/lateral wall MI. We analyzed the severity of LV diastolic dysfunction and influence of atherosclerosis risk factors, infarction site, peak level of cardiac biomarkers such as troponin I, creatine phosphokinase (CPK) and creatine kinase MB (CK-MB), C-reactive protein (CRP) levels, angioplasty effectiveness, reperfusion time, Thrombolysis In Myocardial Infarction (TIMI) and TIMI Myocardial Perfusion Grade (TMPG). An important part of the study was the evaluation of systolic function measured by left ventricular ejection fraction (LVEF) and its correlation with diastolic parameters.

Statistical analysis

Statistical analyses were performed using statistical software Statistica v. 7.1 (StatSoft, Inc. 2001). Continuous variables are presented as mean ± ± standard deviation if normally distributed. Clinical characteristics of the two groups were compared using Student's t-test for repetitive analyses and one-way ANOVA for comparing consecutive continuous variables. Multivariate logistic regression analysis (ANOVA) was performed in order to find the correlation between infarction site, LV filling pattern and continuous variables. χ^2 test was used to measure correlation between LV filling pattern and categorical variables. Statistical significances were defined as p value ≤ 0.05.

The idea of the study was explained to each subject and informed consent was obtained.

Results

Clinical and biochemical parameters were similar in the two groups of patients with anterior and inferior/lateral infarction. Table 1 summarizes the characteristics of the study groups.

Analysis of LV filling pattern showed that on examination E_1 28 patients (28.3%) had normal

Table 1. Characteristics of the patients according to infarction site.

	Anterior infarction (n = 42)	Inferior/lateral infarction (n = 57)	p
Men	33 (78.5%)	46 (80.7%)	NS
Age	53.2 ± 8.7	55.8 ± 7.0	NS
Reperfusion time [h]	4.99 ± 2.41	4.63 ± 2.45	NS
Antropometric parameters			
Body mass index [kg/m^2]	26.3 ± 3.7	27.9 ± 4.2	NS
Body surface area [m^2]	1.94 ± 0.4	1.88 ± 0.2	NS
Clinical parameters			
Heart rate	74.6 ± 16	71.4 ± 16	NS
Heart failure (Killip II–III)	3 (7.1%)	3 (5.2%)	NS
Atherosclerosis risk factors			
Hypertension	64.2%	77.2%	NS
Dyslipidemia	80.9%	70.0%	NS
Low density lipoproteins [mg/dL]	122.23 ± 35.84	131.51 ± 29.92	NS
High density lipoproteins [mg/dL]	43.66 ± 13.73	39.0 ± 10.44	NS
Smoking	62%	61.4%	NS
Positive family history	40.2%	45.6%	NS
Biochemical tests			
C-reactive protein [mg/L]	12.55 ± 12.74	11.55 ± 13.43	NS
Troponine I max [ng/mL]	82.46 ± 66.11	69.69 ± 56.87	NS
CPK max (U/l)	3750.6 ± 3324.4	3031.4 ± 2867.1	NS
CK-MB max (U/l)	351.6 ± 295.1	358.5 ± 403.9	NS

CPK max — creatine phosphokinase average peak level; CK-MB max — creatine phosphokinase MB average peak level

filling pattern (A profile), 45 (45.4%) had impaired relaxation filling pattern (B profile) and 26 (26.3%) presented restrictive abnormalities (C profile). The number of subjects with different stages of diastolic dysfunction seven days after PCI (E_7) were as follows: normal pattern — 27 patients (27.3%); impaired relaxation — 41 (41.4%) and restrictive abnormalities — 31 (31.3%). Three months after primary PCI (E_{90}) 30 patients (30.3%) had normal LV filling pattern, 43 (43.4%) had impaired relaxation and 26 (26.3%) had restrictive dysfunction (Fig. 1).

Hypertension was diagnosed in 71% of patients. Hypertension is known to be one of the factors predisposing to prolonged relaxation filling of LV. We did not prove any correlation between the percentage of hypertension and the progression of diastolic abnormalities during the three month follow-up period (p = 0.822).

During the follow-up period, patients were on pharmacological treatment. All were taking aspirin, clopidogrel and statin. Most were on angiotensin-converting enzyme-inhibitor (96%) and beta-blocker (91%). Analysis of prescribed drugs and their influence on LV filling pattern was not the subject matter of our paper.

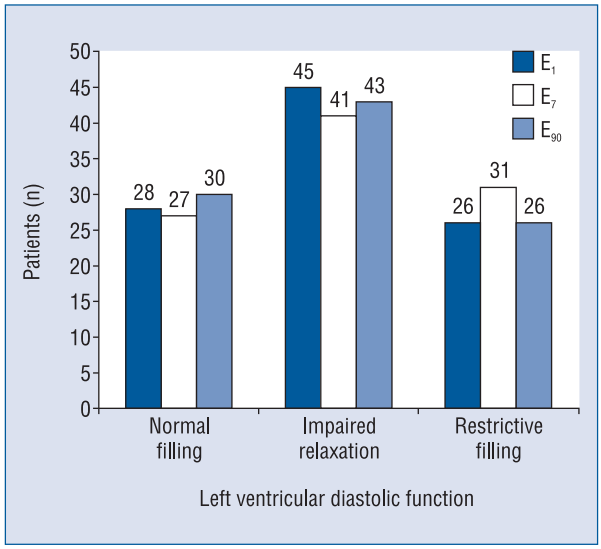

Figure 1. Left ventricle filling pattern in three consecutive echocardiograms: E_1 — examination within one day after myocardial infarction; E_7 — examination on seventh day after myocardial infarction; E_{90} — examination three months after myocardial infarction; pseudonormal/restrictive profile — patients presenting pseudonormal or restrictive filling pattern were evaluated as one group.

Table 2. Left ventricular (LV) diastolic pattern in first echocardiogram (E_1) and coronary artery occlusion site.

LV filling profile (E_1)	Coronary artery segment											
	1	2	3	4	6	7	8	9	10	11	12	13
	Right coronary artery				Left anterior descendent artery					Circumflex artery		
A_1 (n = 28)	5	4	1	1	5	4	1	1	1	3	2	0
B_1 (n = 45)	6	8	6	0	9	7	1	2	0	2	2	2
C_1 (n = 26)	3	2	2	0	6	7	0	1	0	3	2	0
P	0.696	0.502	0.355	0.279	0.891	0.401	0.642	0.981	0.279	0.477	0.825	0.295

E_1 — examination on first day after myocardial infarction

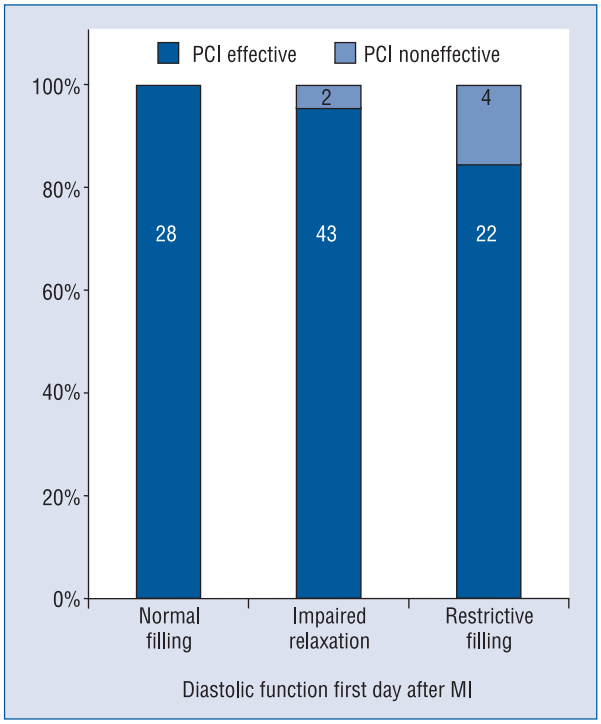

Figure 2. Effective primary percutaneous coronary intervention (PCI) and its relationship with left ventricular filling pattern during the first 24 hours after myocardial infarction (MI).

We demonstrated that primary PCI effectiveness had an influence on the severity of diastolic dysfunction within 24 hours after PCI (E_1) (Fig. 2). Less effective angioplasty was responsible for more evident diastolic abnormalities. We did not observe any correlation between LV diastolic function and TMPG or TIMI scale grading.

Analysis of the infarct related segment of the coronaries showed no specific predilection to any of the LV filling pattern in 1st echocardiogram (Table 2). In the anterior wall infarction group, 18 patients (42.9%) presented impaired relaxation profile and 14 (33.3%) presented restrictive pattern. In the inferior/lateral wall infarction group, impaired relaxation was diagnosed in 27 patients (47.4%) and restrictive abnormalities in 16 (28.0%). Thus we found no correlation between infarct wall and LV filling pattern assessed on the first day after MI ($p = 0.263$).

But we found different results seven days after primary PCI (E_7). Impaired relaxation pattern seven days after primary PCI occurred significantly more frequently in the group of patients with occlusion of the right coronary artery in its proximal part (n = 11, 26.8%; $p = 0.010$). LV filling pattern assessed in E_7 examination was significantly dependent on reperfusion time: in subgroup A_7 reperfusion time was 4.66 ± 1.73 hours, in subgroup B_7 — 4.44 ± 2.19 hours and in C_7 — 5.98 ± ± 3.16 hours ($p = 0.024$) (Fig. 2).

Average values of troponin I max, CPK max and CK-MB max were significantly higher in patients with restrictive filling pattern (C profile) than in those with profile A or B. Similar relationships were observed on the first day after pPCI, seven days later and also three months after pPCI. Correlation between CRP levels and the severity of diastolic dysfunction assessed by left ventricle filling pattern was observed seven days after pPCI (E_7, $p = 0.034$) and three months after pPCI (E_{90}, $p = 0.05$; Table 3).

Analysis of systolic and diastolic abnormalities revealed a close relationship between diastolic function impairment and lower LVEF. Average values of LVEF in patients with restrictive abnormalities (C profile) were significantly lower than in patients with impaired relaxation (B profile; $p < 0.001$) and normal filling (A profile; $p = 0.002$). Left ventricular diastolic profile evaluated at three months after primary PCI showed a correlation with LVEF calculated on E_1 and E_{90} examination (Figs. 3, 4).

Table 3. Average myocardial biomarker levels and C-reactive protein values in patients with different left ventricular (LV) filling patterns.

LV filling pattern	Troponine I max [ng/mL]	Creatine phosphokinase max [U/L]	CK-MB max [U/L]	C-reactive protein [mg/L]
Normal profile (E_1)	69.6 ± 64.1	2862.3 ± 2505.1	269.0 ± 225.1	9.6 ± 6.1
Impaired LV relaxation (E_1)	60.9 ± 50.4	2565.0 ± 2264.6	279.1 ± 195.8	12.6 ± 7.7
Pseudonormal/restrictive profile (E_1)	105.6 ± 65.6	5401.9 ± 3903.4	520.4 ± 292.4	13.5 ± 12.9
Normal profile (E_7)	73.3 ± 67.4	2406.5 ± 2094.2	254.56 ± 211.0	6.7 ± 7.5
Impaired LV relaxation (E_7)	58.1 ± 42.7	2663.49 ± 3015.2	283.49 ± 216.6	12.8 ± 9.3
Pseudonormal/restrictive profile (E_7)	99.3 ± 69.1	5220.71 ± 3110.9	487.97 ± 277.3	15.4 ± 18.9
Normal profile (E_{90})	62.9 ± 60.9	2476.0 ± 2152.6	254.5 ± 202.4	8.2 ± 7.2
Impaired LV relaxation (E_{90})	66.71 ± 52.7	2729.86 ± 2185.0	290.3 ± 188.1	15.4 ± 15.9
Pseudonormal/restrctive profile (E_{90})	103.10 ± 67.0	5552.23 ± 4096.0	519.5 ± 316.9	10.7 ± 12.1

E_1 — examination within one day after myocardial infarction; E_7 — examination on seventh day after myocardial infarction; E_{90} — examination three months after myocardial infarction; pseudonormal/restrictive profile — patients presenting pseudonormal or restrictive filling pattern were evaluated as one group

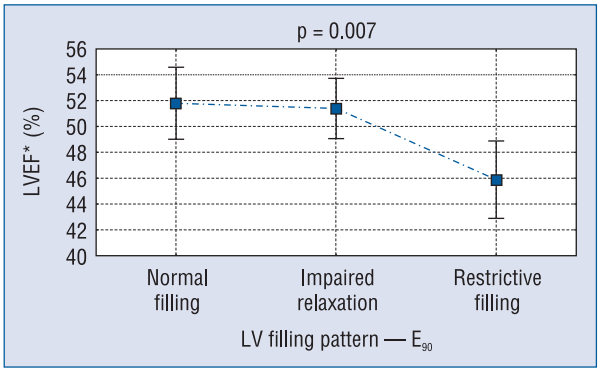

Figure 3. Relationship between left ventricular ejection fraction (LVEF) values on the first day after myocardial infarction and left ventricular (LV) filling pattern three months later; *results assessed within first day after myocardial infarction; E_{90} — examination three months after myocardial infarction.

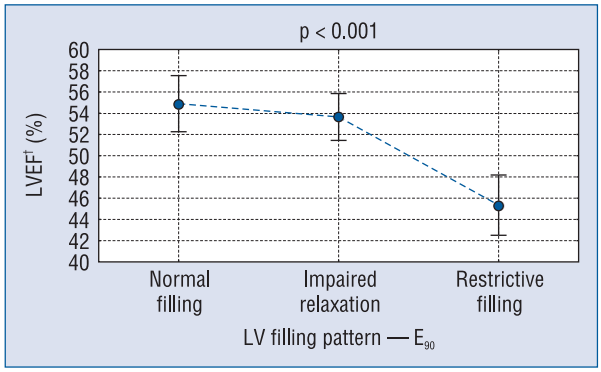

Figure 4. Relationship between left ventricular ejection fraction (LVEF) values and left ventricular (LV) filling pattern three months after myocardial infarction; †results assessed three months after myocardial infarction; E_{90} — examination three months after myocardial infarction.

During follow-up between E_1 and E_{90} examinations left ventricular filling pattern was stable in 62 patients (62.6%), left ventricular diastolic abnormalities progressed in 17 patients (17.2%) and LV diastolic dysfunction improved in 20 patients (20.2%). In these groups we compared changes of left ventricle end-diastolic volume during observation. Patients presented dilatation of LV in control echocardiogram three months after MI: those with progression of LV diastolic function: 62.88 ± 18.74 mL; those with stable filling pattern — 62.90 ± 27.50 mL; and those with improvement of LV filling pattern — 60.23 ± 20.83 mL. We did not observe significant differences between groups (p = 0.901),

Discussion

Our study showed that 71.7% of patients with STEMI treated with primary PCI present left ventricle diastolic dysfunction on the first day of MI. Three month follow-up showed that relaxation abnormalities were most common. This type of LV filling abnormality occurred in 46% of patients on the first day of MI, 41% of patients seven days later and 43% of subjects three months after pPCI. Poulsen et al. [9] obtained similar results, demonstrating impaired relaxation in 40% of patients three months after MI.

Significantly more examples of occlusion of the proximal right coronary artery were identified

among patients with impaired relaxation of LV at seven days after pPCI (E_7; n = 11, 26.8%; p = 0.010). In the literature there are no reports on the association between the site of coronary artery occlusion and changes in diastolic function. It is likely that impairment of relaxation in patients with inferior wall MI corresponds to LV diastolic asynchrony in that specific infarct location.

Structural changes in the left ventricle as a result of healing and remodeling after myocardial infarction may lead in a few months to myocardial stiffness and elevation LV filling pressures. Only segments of frozen or hibernated muscle may return to its proper function in case of effective revascularisation [12, 13]. These changes may help explain the presence of LV diastolic abnormalities in a large number of patients (69%) as late as three months after reperfusion therapy for myocardial infarction.

The higher rate of effective reperfusion treatment correlates with the lower rate of heart failure developed as a result of myocardial infarction [14, 15]. In our study we found a close relationship between LV filling profile on the first day of MI and effectiveness rate of mechanical reperfusion (p = 0.05). Reperfusion was found to be 100% effective in patients with proper LV filling and only in 84.26% of patients with restrictive abnormalities. That type of correlation did not play a role three months after MI which could be accounted for by the contribution of other factors to the remodeling process after MI.

There is evidence confirming a strong relationship between necrotic area and the severity of left ventricle diastolic impairment. Orn et al. [16] reported an analysis of data obtained via Cardiac Magnetic Resonance in patients with myocardial infarction treated with mechanical revascularization in the OPTIMAAL trial. They proved that changes in left ventricle end-diastolic volume and the lowering of ejection fraction showed a linear relationship with the necrotic area. In contrast, the alterations did not correlate with transmurality of MI and infarct site [16].

Average levels of troponin I max, CPK max and CK-MB max were significantly higher in patients with restrictive filling pattern (C profile; p = 0.007). There were no significant differences between groups with normal filling and impaired relaxation (p = NS). The same relationships were observed on E_1, E_7 and E_{90}. It confirms the importance of the extension of the necrosis area as a predictor of diastolic abnormalities in the early phase of MI.

The analysis of left ventricular function showed a close relationship between diastolic function abnormalities and systolic dysfunction [17]. Average values of LVEF in patients with restrictive filling pattern (C profile, 44.7%) were significantly lower than in those with impaired relaxation (B profile; 52.7%; p < 0.001) and normal filling (A profile; p = 0.002). Comparison of LVEF between subjects with impaired relaxation and normal filling revealed no differences. Left ventricle filling profile evaluated three months after primary PCI correlated with LVEF on the first day after MI and three months after pPCI. Poulsen et al. [18] obtained similar results. They accounted for these differences by a higher extension of the necrotic area in subjects with restrictive abnormalities.

The findings in patients in the early phase of STEMI treated with primary PCI confirm the importance of the inflammatory response in the development of diastolic abnormalities. The inflammatory reaction was reflected by higher CRP levels. The correlation between CRP levels and left ventricle filling pattern was observed at seven days after pPCI (E_7) and three months after pPCI (E_{90}, p = 0.034; p = 0.05).

The present findings suggest that impairment of left ventricular diastolic function in the early phase of STEMI infarction plays an important role in the clinical evaluation of patients treated with primary PCI.

Conclusions

More than half of patients with a first STEMI infarction have left ventricle diastolic dysfunction within the first day after PCI; and these abnormalities are still present three months after PCI. Time and effectiveness of reperfusion, CRP level, troponin I max, CPK max and CK-MB max levels, as well as LVEF, have an important influence on the development of diastolic dysfunction. Infarct extension contributes significantly to the process.

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